RICHARDSON (Jos. G.)

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A LECTURE

ON THE

TRUE NATURE AND ORIGIN

OF THE

SALIVARY GLOBULES,

AND THEIR

IDENTITY WITH THE WHITE CORPUSCLES OF THE BLOOD.

By JOSEPH G. RICHARDSON, M.D.,

LECTURER ON PATHOLOGICAL ANATOMY IN THE UNIVERSITY OF PENNSYLVANIA, AND MICROSCOPIST TO THE PENNSYLVANIA HOSPITAL.

(Delivered before the Odontographic Society of Pennsylvania, Nov. 5th, and before the Pennsylvania Association of Dental Surgeons, Dec. 9th, 1873.)

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The human mind, under conditions of culture and refinement, discovers few more agreeable occupations in the various departments of that greatest of all means of happiness, *the exercise of power*, than in exploring the mysteries of natural phenomena, and unveiling the hidden structure and constitution possessed by the innumerable objects which surround us in the world.

This desire for investigating the secrets of creation, like certain other less satisfying passions, grows with what it feeds upon, and I therefore confidently hope that your attachment to the school of seekers after truth in nature, will lead you to feel an interest this evening in my remarks upon the true structure and origin of the salivary globules, and their identity with the white corpuscles of the blood; particularly as these researches have a direct bearing upon some of the knotty problems in your own specialty of medicine.

The nature of the nucleated corpuscles so abundant in the saliva has long been a subject of some uncertainty; and although they have, no doubt, as favorite test-objects for the higher powers of the microscope, been more frequently examined by microscopists than almost any other constituent of the glandular secretions, observers seem to have been generally contented to accept them simply as useful measures for the capacity of the higher objectives, and passed on without attempts to solve the enigma of their origin.

The celebrated German histologist Kölliker has indeed advanced the theory that they are essentially a form of exudation-corpuscles, but his hypothesis does not appear to have been accepted by microscopists generally as a fixed fact; for, although Messrs. Griffith and Henfry, the able authors of the Micrographic Dictionary, published in London, 1860, remark that this view (of Kölliker) is probably correct, for they may occur in the secretion of any mucous surface, and have no special connection with the salivary glands, Prof. Lionel Beale, writing in 1867, observes: "The examination of the saliva presents no difficulty. The fluid is perfectly transparent and viscid, but holds in suspension, besides epithelium from the mouth, a number of small cells, for the most part of an oval or spherical form, which are probably derived from the ducts of the gland. They are about one-two-thousandth of an inch in diameter, and are sometimes called 'salivary corpuscles.' In some cases they accumulate in great number, and closely resemble pus-corpuscles. Some observers consider them to be altered epithelium from the cavity of the mouth; but this can hardly be the case, as they are often met with in the absence of any of the characteristic cells of scaly epithelium. They are found in great number in cases of salivation. In the somewhat viscid matter of which the salivary corpuscle is composed are multitudes of highly refractive particles, in incessant motion. The nature of these particles is extremely doubtful. They look very like the germs of Bacteria, and it is possible they may be of this nature."

According to my own observations, first published in the Pennsylvania Hospital Reports for 1869, "The salivary corpuscles prepared for examination (by merely placing a drop of saliva on a slide, covering it with a very thin glass), and observed under a power of eleven hundred diameters, present the appearance of perfect spheres, varying from $\frac{1}{1400}$ to $\frac{1}{2500}$ of an inch in diameter, each having a very transparent but beautifully-defined cell wall of exceeding tenuity, which incloses from one to four almost equally transparent nuclei (of a circular or oval form), whose diameters range from $\frac{1}{3000}$ to $\frac{1}{4000}$ of an inch or even less. These nuclei are situated sometimes centrally, but more commonly near one side of the corpuscle, and the cavity between their margin and the cell wall is generally filled with from twenty-five to fifty molecules not more than $\frac{1}{20,000}$ of an inch in diameter, whose characteristic is that of constant and rapid motion. Some of these molecules seem to be elongated into an oval or hour-glass form, but the activity of their movements renders it difficult to ascertain this with precision. In my observations the corpuscles themselves have appeared to enlarge and become flattened from the pressure of the glass cover, as the stratum of liquid beneath it grew thinner from marginal desiccation, so that usually in the course of an hour or so they

burst and discharge one-fourth (or more) of their contents, when two, three, or more of the molecules swim away, continuing their revolving movements until they pass out of view; the other granules outside, and those remaining within the cell, become in a very few seconds entirely stationary. If a solution of aniline red, of the strength of one grain to the ounce of distilled water, be allowed to penetrate at the margin of the cover, the nuclei of the salivary corpuscles are readily stained of a bright crimson, and are thus exhibited with beautiful distinctness. The dye appears, however, to exert an immediate influence upon the movement of the molecules, as I have rarely been able to find cells in which these continued to move after the nuclei became at all colored."

Before proceeding to narrate the curious accident which led me to the discovery which forms the main subject of my lecture, I think it will be interesting to you for me to quote some remarks of Prof. Kölliker, as showing how nearly a man of great genius may approach the truth and yet fail to grasp it, through being withheld by the influence of some false general doctrine: in this case, the erroneous dogma of an essential difference between the pus- and white blood-corpuscles.

The salivary or mucous corpuscles, says he, are "rounded, of 0.005 of a line in diameter, with one or many nuclei, always to be met with in the fluid of the mouth, and usually supposed to be derived from the mucous or salivary glands, yet wrongly, since the examination of both these kinds of glands and of their ducts teaches us that they excrete no formed elements. In my opinion," continues he, "these corpuscles are nothing but products of the mucous membrane of the oral cavity; not normal, although they are almost constant; but a kind of exudation- or pus-corpuscles, with which they have, as is well known, the closest possible resemblance in structure. Many authors consider them to be abortive epithelial cells of the oral cavity; but if that were true, the epithelium of the localities in which they are found must want the outermost layer of large flattened scales, *which is by no means the case.* In my own person, at any rate, I find these mucous corpuscles on the gums, lips, cheeks, and tongue, in localities in which the epithelium is wholly uninjured; and by scraping with a knife I can often obtain entire lamellæ of epithelial plates, covered with mucous corpuscles. I do not mean to affirm by this" (and here I beg you to notice, gentlemen, how Kölliker retreats from the verge of the important discovery near which he has strayed, driven back by the false doctrine that a peculiar exudation gives rise to distinctive pus-corpuscles),—"I do not mean to affirm by this," he says, "that in little sores arising from whatever cause, upon the gum, for instance, where the epithelium is wholly or partly wanting, or when it is lost more extensively in consequence of disease, that mucous or exudation-corpuscles may not be developed as upon other sore surfaces, and these might be regarded

as abortive epithelium cells, but only that this does not take place in the oral cavity under ordinary circumstances. I consider, therefore, that the so-called mucous or salivary corpuscles are exudation-corpuscles, and consequently totally distinct from epithelial cells, and I regard their formation to be analogous to that of pus-corpuscles in catarrh, which also very often takes place upon unbroken epithelial surfaces. It is thus readily explained how it is that they are almost entirely absent in many individuals, while in others who are subject to irritation of the mucous membrane of the mouth they are very abundant; likewise we may see how it is that they have been observed in saliva obtained from a fistulous aperture."

The circumstance already alluded to, as conducting me to what I believe to be a correct view respecting the origin of the salivary globules, was as follows: In examining some of the renal secretion obtained on the 8th of August, 1868, near my former residence in western New York, from a patient who complained of severe pain in the kidneys and bladder, I was surprised to find that a deposit which appeared to the naked eye purulent was chiefly composed of cells exactly resembling in form, size, definite cell wall, contained nuclei, and actively-revolving molecules, the salivary corpuscles with which by frequent observation I had become so familiar; and should have imagined that these proceeded from an accidental adulteration with sputum, had I not been fortunate enough to have ocular demonstration to the contrary when procuring the specimen. I examined these corpuscles repeatedly in the course of the two following days, during which the movements of the molecules continued, but could make nothing else of them except drawings, which were carefully preserved.

Numerous investigations of specimens from a great variety of cases, during the succeeding months, failed to reveal any more of these globules for which I was so eagerly searching; but in December of the same year I met with them again in the renal secretion from another case of cystitis; and a few days afterwards, whilst examining another sample from a patient affected with the same disease, observing that some of the pus-cells it contained had a spherical outline, were almost opaque, and only about $\frac{1}{3000}$ of an inch in diameter, it suddenly occurred to me that they were perhaps merely contracted by the exosmose of their fluid contents into the surrounding denser medium, and the idea suggested itself to me to try the effect of diminishing the specific gravity of the urine by the addition of water. Under this treatment I found that the cells of the pus, which had been exhibiting amœboid movements, soon assumed a spherical shape, rapidly enlarged until they reached the diameter of about $\frac{1}{1700}$ of an inch, when the contained molecules began to revolve, and ere long took upon themselves the extremely rapid and confused movement which I had twice

before seen in similar cells deposited from the renal secretion, and hundreds of times in the salivary globules. The action of aniline solution resulted in rendering visible beautifully distinct, definite nuclei, analogous to those found in the salivary bodies.

About this time, as many of you will remember, appeared the announcement of Prof. Cohnheim's remarkable researches, establishing the identity of white blood- and pus-corpuscles in the frog; and the opportunity of at least partly corroborating them in regard to human beings thus obviously presenting itself, I contrived the following experiments for that purpose:

Drawing a drop of blood from the tip of my finger (by puncture with a cataract-needle) upon a glass slide, to which was attached a small reservoir composed of the lower half of a two-drachm vial, I covered it with thin glass, and placed it upon the stage of the microscope. After finding a white blood-corpuscle showing well-marked granules and well-characterized amœboid movements, I raised the objective out of the way, and arranged a fine filament of thread to act as a syphon from the little reservoir (previously filled with fresh water) to the upper edge of the cover, and a fragment of moistened paper to the lower, according to the usual method of securing a constant current beneath the thin glass. On depressing the body of the instrument, and thus bringing the corpuscle again into view, I found it still adhering to the under surface of the cover, notwithstanding the torrent of red globules hurrying across the field; and as these became paler and less distinct through exosmosis of their colored contents by reason of the diminished density of the serum (which of course was all the time being diluted by the water conveyed to it by the miniature syphon), the white cell first gradually expanded, and displayed its delicate wall, with two rounded nuclei; then, after acquiring the magnitude of $\frac{1}{1700}$ of an inch, it exhibited the rapid and incessant movement of its contained molecules; and finally, when its diameter reached about $\frac{1}{1400}$ of an inch, it burst suddenly, discharging a portion of its contents, whose outbreak resembled that of a swarm of bees from a hive, and some particles of which, actively revolving as they went, swam off to the confines of the microscopic field. On repeating the observation, and allowing some aniline solution to flow in with the water, after the first few minutes the nuclei were strongly stained and rendered beautifully distinct, although the movement of the molecules promptly ceased; in this respect, as in all others, showing, so far as observed, a precise identity with the reaction afforded by the pus and the salivary corpuscles, as already described.

This investigation can be very readily repeated by any one who possesses a microscope and a good $\frac{1}{10}$, or even $\frac{1}{8}$ inch immersion objective; and as it is the turning point upon which, supported by other researches,

my doctrine of the salivary corpuscle rests, I am very anxious that all of you who have time and opportunity will test the correctness of my description of the phenomena it reveals, by actual observation; and I would here remark that if any of my auditors finds a difficulty in carrying out these suggestions, or arrives at conclusions at variance with mine, I hope he will give me an opportunity to go over the process with him, and endeavor to demonstrate that absolute truth in regard to the matter for which I believe we are all seeking, as far as possible without prejudice and without fear.

Assuming now, for the sake of the argument, that the facts detailed above, and which I again beg you will examine for yourselves, concerning the changes occurring in white blood-corpuscles, or, as I prefer to call them, leucocytes, when immersed in a fluid of the low specific gravity of the saliva, are correctly stated, it is obvious that they afford ground for a strong presumption that these leucocytes, which we know are always circulating by tens of thousands in blood-vessels which ramify within one-fiftieth of an inch of the free surface of the mucous membrane lining our mouths, do escape in some mysterious way from the vessels, and enter the oral cavity, where the saliva distends them in the same manner that water does in our experiment; further, that when thus enlarged, they constitute the salivary globules without other alteration than that of magnitude, their identity remaining undisturbed, just as a patient who becomes dropsical continues to be the same individual after the most profuse effusion which his skin will contain takes place, even although his body and limbs are rendered double their normal size, and their normal movements are impeded or annulled.

In order to establish such presumption of the identity of the dropsical and non-dropsical leucocytes into a fact, I must, however, ask your attention to a brief account of the nature of this latter important histological element (upon which I had the honor to report to the American Medical Association at its meeting in this city last year), and also to the vital part it performs in the inflammatory process.

If we attempt to penetrate the mysterious phenomena displayed in the early stages of embryonic life, we find, as I need scarcely remind you, that the first change which occurs in the impregnated ovum of all animals is, to quote from Dr. H. C. Chapman's excellent "Evolution of Life," that the globular vitellus or yolk "divides into two segments, each segment having a nucleus with its nucleolus. These two segments subdivide into four balls, the four into eight, the eight into sixteen, and so on. Through this process of cell-division, or segmentation as it is called, the vitellus is divided into a number of little balls, and assumes the shape of a mulberry. Finally the superficial balls of the mulberry are transformed into cells, and so arrange themselves as to present the

appearance of a mosaic pavement; as the deeper balls become cells they pass to the surface, and increase the thickness of this mosaic-like membrane. In this way the vitellus is converted into a vesicle ; within this vesicle there shortly appears a second vesicle ; (the walls of) these two vesicles are usually called the germinal layers, or the external and internal blastodermic membranes." Between these two soon after developes another stratum of cells, called the middle blastodermic layer or hæmoblast, because it is the source of the blood and vascular apparatus.

Now, gentlemen, the small round cells, which in uninterrupted accumulation form in the impregnated ovum the germinal disk and germinal area, at a little later period constitute the external, middle, and internal blastodermic membranes, and still later differentiate into the blood and its vessels, are on the one hand thus the progenitors of the white corpuscles or leucocytes of the blood, concerning which I shall have so much to say to you, and on the other most closely resemble these same white blood-corpuscles, and likewise the cells of inflammatory lymph (the reparative material provided by nature for the healing-up of wounds) and the corpuscles of freshly-formed pus, all of these morphological elements being typical examples of that active protoplasm which Prof. Huxley has rendered so famous, under the title of "the physical basis of life."

Hence you perceive, I doubt not, the great importance of a complete knowledge, as far as possible, of these cellular elements, not only for my present purpose of proving to you the identity of leucocytes generally with the salivary globules, but also to our studies as anatomists, physiologists, and embryologists; and you are therefore prepared, I trust, to follow me into an investigation of their minute structure and physical properties, as most conveniently displayed for examination, in the white corpuscles of the blood. If you puncture the ball of your finger with a quick stab of a cataract- or ordinary sewing-needle, press out a small drop of blood the size of a yellow mustard-seed, touch the middle of a glass slide to this drop as it projects from the surface of the finger, and then lay the ensanguined spot of the slide gently upon a thin glass cover, which has been carefully cleansed, you will have, on inverting it, a specimen suitably prepared for the examination of the leucocytes of blood.

Under a microscope affording a power of two hundred and fifty diameters you will soon discover, on attentive examination among the piles of red corpuscles which cover the field, some five or ten roundish, oval, or irregularly-shaped masses of grayish-white color and finely-granular aspect, contrasting in both these qualities in a marked manner with the homogeneous yellowish-red disks. These are the white blood-corpuscles or leucocytes, which may be studied, and their wonderful

amœboid movement recognized, under a quarter-inch lens, but require for their satisfactory investigation a $\frac{1}{10}$, $\frac{1}{16}$, or $\frac{1}{25}$ immersion objective.

The white cells of the blood were first distinguished from the red disks by Hewson, about 1775, but do not appear to have attracted much attention from pathologists until near the middle of the present century, when William Addison, in 1843, published his second series of experimental researches on the actual processes of nutrition, in which he asserts their importance as constituting the cellular elements of both tissues and secretions. His observations were followed by those of Wharton Jones and Augustus Waller, in 1846; Von Recklinghausen, who examined the amœboid motion of leucocytes in 1863; Max Schultze, who studied these remarkable movements under the influence of artificial heat in 1865; and Cohnheim, whose great doctrine of inflammation, as the result of a "wandering out" of "migrating" white corpuscles, through the stomata of the vessels, was promulgated in 1867, since which time the leucocytes of the blood have been special objects of investigation to microscopists throughout the world.

This remarkable discovery of Cohnheim, affording the second great link in my chain of argument to prove the identity of the salivary and white blood-corpuscles, by demonstrating how the latter make their way through the vascular walls, and, wandering through the tissues, are set free in the oral cavity, is briefly as follows:

In the course of his investigations upon inflammation, Prof. Cohnheim found that if we take a frog paralyzed by the injection of curare (the South American woorara) or of chloral, and, incising the abdominal parieties, draw out a portion of the intestine, so that the thin membrane of the mesentery can be spread out beneath the microscope, it is easy to watch the whole inflammatory process (which is soon set up, in consequence of exposure to the air) from its very commencement.

After the primary steps of inflammation, namely, the irregular dilatation of the vessels and the slowing or complete stasis of the blood-stream, well known to older experimenters, we observe that the leucocytes roll lazily along upon the inner surfaces of the smaller veins (and to a less extent of the arteries), where they soon begin to adhere.

On fixing our attention upon one of these adherent white blood-cells which is favorably placed for observation, we may see that in a short time it begins to display the curious amœboid movement, shooting out a tongue-like process apparently into the wall of the blood-vessel, but in reality into one of the minute pores or stomata which, as I shall show you presently, everywhere stud the boundaries of the vascular system. Continuing our scrutiny, we observe that this tongue-like projection of the substance of the blood leucocyte becomes club-shaped or knobbed at its outer end, and that this bulging of the extremity goes

on increasing, the main mass of the leucocyte meanwhile diminishing in an inverse ratio, until the whole corpuscle assumes a dumb-bell shape, one of the terminal dilatations being within, and the other outside of the vascular wall. Finally we notice that the internal knob of the dumb-bell grows smaller, whilst the external one becomes *pari passu* larger, until the former entirely disappears, and the connecting band or bridge (corresponding to the shank of the dumb-bell) being likewise ultimately withdrawn into the main mass of the corpuscle, the entire leucocyte severs all its connection with the blood-vessels, whence it has thus emigrated, and we may see it wander away among the connective-tissue cells, which go to make up the substance of the surrounding structures.

The stomata or pores of the finer blood-vessels, to which I have already alluded as playing such an important part in this process, as giving exit to the migrating leucocytes, are minute apertures, varying from $\frac{1}{10.000}$ to $\frac{1}{20.000}$ of an inch in diameter, and occurring at the lines of junction of two or three of the broad irregularly-shaped epithelial cells which form the endothelial lining of the vascular system. They are best demonstrated by defining these endothelial cells with $\frac{1}{2}$ per cent. nitrate of silver solutions; and I show you here an exquisite photograph of such a preparation, for which I am indebted to my friend Col. J. J. Woodward, of the Army Medical Museum at Washington. In it (No. 3378 Microscopical Section) you see the irregular zig-zag lines of junction of the endothelial cells, reminding one of the sutures in the cranial bones, and at certain points, designated by pencil-lines, the holes or stomata which have just been described.

I am accustomed to demonstrate this most important part of the inflammatory process to my classes in Pathological Anatomy at the University of Pennsylvania, by the simple models you see here.

In this ball of soft putty you have an almost exact representation of a white blood-corpuscle when magnified 5000 diameters; and if you examine a favorable specimen of the living leucocyte, on a slightly-warmed slide, as already suggested, you will see it after a short time (as I show you here) desert its globular shape by sending out a tongue-like process, and then gradually growing into this, as it were, until, passing through the dumb-bell and tadpole forms, it may resume its spherical shape, after traveling a distance equal to its own length across the field. This snail- or worm-like motion is the wonderful amœboid movement of which you hear so much, and which it is capable of performing continuously, under favorable circumstances, for a period of at least two days after being deposited upon a glass slide.

Under comparatively low powers, such as the $\frac{1}{4}$ or $\frac{1}{5}$ inch objective, giving an amplification of 200 or 250 diameters, it is difficult to see all the steps of this movement of the leucocyte; but by close watching

it is quite possible to detect slight modifications of shape, and, after a proportionate length of time, some perceptible alteration of position.

To illustrate the entire process of emigration of the leucocytes as seen in Cohnheim's experiment, I will ask your attention to this tin tube, about three inches in diameter and eight inches long, upon whose exterior I have painted the outlines of the endothelial cells (with their nuclei stained with carmine), *as they actually existed* in the small vein from which Dr. Woodward took the photograph already shown you. At one point I have perforated the tin (just as one of the stomata does the coat of the blood-vessel), and through that aperture you can see me thrust a small ball of putty, representing a white blood-globule on its way as it "wanders out" to constitute a corpuscle of pus. During its journey from the inside to the outside of the vein it assumes, you observe, first a tadpole shape, with the tail pointing externally, then a dumb-bell or hour-glass outline, and finally a caudate form again, with the tail directed internally, however, exactly as I have described to you the leucocytes do in the celebrated investigation of Prof. Cohnheim.*

Now, gentlemen, when you remember that in order to permit of this emigration of the white blood-cells it is not necessary that actual inflammation, with complete interruption of the circulation, should occur, but that it may take place as a consequence of partial stasis of the blood-stream during mere congestion, you will, I think, perceive at once that this discovery of the talented German pathologist has within the last few years, and within them only, opened the way for an acceptance of such a theory as mine, by revealing to us a simple and natural method by which the leucocytes of the blood may escape from within the vessels, and, making their way through the thin layer

* A comprehension of this "wandering out" of the leucocytes enables us to explain the various phenomena of inflammation, about the mouth as well as elsewhere, with wonderful beauty and clearness. Thus, for example, when you attempt to fill the pulp cavity of a tooth after destruction of the nerve in the root, and before the irritation in the stump of that nerve has subsided under treatment, the gradually increasing pain felt by the patient is due simply to the escape of twenty, fifty, or perhaps a hundred thousand white blood-corpuscles, which wander out through the stomata of the vessels, as I have demonstrated above. Since these must have room in the bony canal into which they emigrate, they necessarily compress the remaining nerve-tissue at the foramen, and cause, as mechanically as the atrocious thumb-screw of the inquisition, first the tension, then the pain, and finally the excruciating agony which attend an abscess at the root of a tooth. Of course the obvious remedy of removing the plug and giving exit to the tiny drop of pus (made up of these emigrating leucocytes) acts not by preventing white blood-corpuscles from wandering out at various points of the inflamed vessels, but by obviating that *painful pressure* which these little wanderers seem to have the power of producing whenever and wherever *imprisoned*, and so restricted in the exercise of their extraordinary amœboid movements.

of tissue lining the oral cavity, be set free upon its surface, where they undergo almost immediate distension, and become the corpuscles of the salivary fluid.

But lest there be some skeptical individuals among you, who doubt whether the white blood-corpuscle swells into a salivary globule (because no microscopist has ever seen that entire change in all its stages) without changing *its* identity; and also doubt whether the human ovulum, after it escapes from the Graefian follicle, still retaining *its* identity, undergoes development into a fœtus, *for the same reason*, I have still in reserve a method of proof, which, borrowed as it is from mathematical demonstration, seems to me to afford an approach to mathematical cogency in its conclusiveness.

If a dropsical patient, so swelled by serous effusion that, to use a vulgar expression, his own mother would not know him, wished to establish *his* identity, it is manifest that one of the most available methods would be to get rid of the fluid by which his form and features were distended, and so restore his lineaments to their normal aspect. In like manner it occurred to me that if we could withdraw that excess of fluid (carried by endosmotic action into the leucocyte) which by mere mechanical enlargement causes it to become spherical and to assume the salivary corpuscular form, we would be able to restore to it the well-known aspect of a white blood-corpuscle, and so contribute an important item of evidence to the support of my theory. An investigation like this would, as has been remarked in an editorial upon the subject in the DENTAL COSMOS, "seem to adapt to the solution of the problem the schoolboy's method of proving a sum in simple addition, by subtracting from the total one of its constituent quantities, and obtaining the other as a remainder."

Such indeed is the case, as is proved by the following experiment, which I likewise beg any doubters to repeat, and verify or disprove for themselves.

In the course of investigations upon the character of the white blood-corpuscles in my report above mentioned, I removed a small portion of tartar from between two of the molar teeth, placed it upon a slide, and adjusted it beneath the microscope as already described for examination. After some search, a bay-like indentation in the margin of the tartar was found, occupied by a mass of some fifty salivary corpuscles, nearly all exhibiting the dancing motion of their molecules in great perfection. On introducing a current of the three-quarter per cent. common salt solution (by means of the thread syphon as explained in an early part of my lecture) these globules rapidly *contracted*, the molecular movements in their interior ceasing, when they were about $\frac{1}{2000}$ of an inch in diameter, in a reluctant manner, apparently in part because the granules had no longer space to vibrate in

the contracted corpuscles, and in part because the fluid in which they floated within the leucocytes became too viscid to permit such vibration. When the salivary globules were reduced by this abstraction of water to a diameter of about $\frac{1}{2500}$ of an inch, well-marked and unmistakable amœboid movements were seen to occur in several instances; and since this power of amœboid motion is the most characteristic property of the white blood-corpuscles, I thus obtained the same kind of proof of their identity with the blood leucocytes which our supposed dropsical patient would do if by a course of diuretic medicines he were to get rid of the superfluous water, and regain his original form and power of movement.

From these various data I deem we are justified in concluding that, tracing the white blood-corpuscle from its condition of irregular outline and amœboid movement as observed in the liquor sanguinis and in heavy urine, through its rounded form with slightly more distinct nuclei in the liquor puris of pus not perfectly fresh, and in urine of lower specific gravity, we find that, immersed in a rarer liquid approximating to the mean density, or at least the osmotic power, of saliva, it has an accurately spherical outline, is more than twice its original magnitude, and contains a number of minute actively-moving granules, thus exactly resembling in all sensible characters the true salivary corpuscle. Hence I maintain "that the blood under the appointed nervous influence, congesting the buccal mucous membrane and associated glands, moves slowly enough through their capillaries to allow some of its white globules to penetrate the walls, as they are seen to do those of the frog's mesentery in Cohnheim's now celebrated experiment." Further, that these very leucocytes, after coming under the influence of the rarer saliva, which expands them and sets free to move their contained molecules, "constitute the bodies so long known to histologists as the corpuscles of the salivary fluid."

My researches heretofore alluded to lead me to conclude that the white blood-corpuscle (which I hope you are now all willing to recognize and desirous of studying as a *non-dropsical salivary globule*) is a cell, composed of, in the first place, a nucleus (or nuclei) which possesses the power of independent amœboid movement, and is insoluble in water, but capable of slowly imbibing that fluid until swollen to nearly double its normal size. The cell wall of the corpuscle is a membranous envelope insoluble in water even when boiling, too thin to exhibit a double contour with a magnifying power of 1200 diameters, but firm enough to restrict the movement of its contained granules within its limits. Its exterior is adhesive, so that surfaces or particles coming in contact are liable to become attached thereto. Some phenomena observed lend countenance to a theory that these membranous parieties are dotted with minute pores, which permit delicate

threads of the inclosed soft protoplasm to be extended, and that the edges of these foramina, if the projection still continues, are carried outwards during the amœboid movement, forming a sheath to all except the extreme point of the tongue-like process. The material occupying the space between the capsule and the nucleus, denominated the protoplasm of the cell, is a soft jelly-like matter, in which chiefly resides the capacity of amœboid motion. The protoplasm seems to be soluble in water and saline solutions in all proportions, and when freely diluted loses its amœboid power, which, however, is strangely enough regained in a majority of instances when the excess of liquid is removed.

The laws by which leucocytes take up and part with their fluid seem to be simply those of the dialysis of liquids through animal membranes, by endosmosis and exosmosis, as investigated by Graham in 1855; the rapid inward current from the rare solution, or at least the solution of high diffusive power, through the cell wall, distending that membrane and diluting the contained fluid, until an equilibrium of the endosmotic and exosmotic flow is attained, or the capsule is burst by the centrifugal pressure of accumulated liquid.

The structure of the particles which exist in the protoplasm and exhibit dancing motions when the latter undergoes dilution is yet undetermined, although sundry facts indicate that their movement is not dependent on "vital" causes, but is merely a molecular one, also that some of them at least are minute granules of fatty matter, which after a time may coalesce into visible oil globules, as in the older pus-corpuscles. In regard to any difference of their motion in the salivary bodies, my experiments so fully and uniformly corroborate each other that, reluctant as I feel to dispute the assertions of such celebrated histologists as Stricker and Pflüger, I cannot but call in question the general correctness of their statement upon this point, for it is manifestly inaccurate to affirm, as they do, that a half to one per cent. salt solution still permits the "dancing" movements of fresh pus- or lymph-corpuscles to continue, whilst it abolishes those of the salivary globules, when the fact is that the motion ceases in nineteen out of every twenty corpuscles under its action; just as it would be erroneous to maintain that quinine does not stop the course of ague, because in one case out of twenty it fails to prevent a recurrence of the chill.

Touching the vexed question of a cell wall to the leucocytes of blood, pus, saliva, etc., I may remark that although Stricker and Brücke express themselves with such decision in recent papers respecting the necessity of detecting a double contour at the periphery of a cell before the presence of an investing membrane can be admitted, it seems to me that the recognition of such a duplicate outline is a question not solely of the existence of membrane, but also of its thickness. It will, I presume, be readily acknowledged that many films of tissue

exist in animal bodies, as for example the arachnoid during fœtal life, which are of such tenuity that in a transverse section the naked eye or even a magnifying power of ten diameters can discern but a single contour; and yet no man in his senses will deny that such membranes have a positive existence. Furthermore, histology teaches us that other membranes occur, which are but one-half or even one-tenth the thickness of the human arachnoid. These consequently can exhibit but a single contour when magnified twenty or one hundred diameters respectively, and yet it is easy to demonstrate that they are real, not imaginary, structures. Since, therefore, our knowledge does not warrant us in asserting that membranes must *necessarily* be more than $\frac{1}{50.000}$ (for example) of an inch in thickness, any more than we are able to say that hairs must be over $\frac{1}{50.000}$ of an inch in diameter, or they do not exist, I cannot think that inability to detect, with the lenses now in use, both an inner and outer border to the boundary of a cell, is sufficient foundation for denying the presence of a proper cell wall, and believe this difficult question must be determined, if at all, by other and independent testimony.

Of such decisive character are, it appears to me, the dancing movements in certain cases, where, but few molecules being present, individual particles may be selected for observation, and (as I have frequently noticed) distinctly seen to swim rapidly in a centrifugal direction until they strike the single contoured boundary line of the cell, from which they *rebound* sometimes for a distance equal to one-fifth the whole diameter of the corpuscle. Also I think the surprising rotary motion which I have described as occurring after the action of ferrocyanide of potassium solution even more conclusive, for it appears almost incredible that both molecules and nuclei could quickly revolve within the limits of a cell, unless they floated in very liquid cell contents, or again, that a cell made up of fluid so rare as to permit particles to move through it with such velocity, could either retain its oval shape or restrain its rotating molecules within its limits, except by the aid of a membranous wall of considerable firmness. To recur to a simile which I have elsewhere used in reference to the red blood-disk, it seems to me that this hurried rotation of granules and nuclei inside of a white blood-corpuscle furnishes the same kind of proof that it possesses a cell wall, as the swimming of a shoal of little gold-fish around the inner surface of their vase affords us, first, that they float in liquid instead of being imbedded in jelly, and second, that *they* are confined by a boundary wall, firm enough, not only to prevent them from passing beyond its limits, but also to retain its shape, in spite of the pressure of the liquid within its cavity.

Summing up now the results of these various researches, you per-

ceive that, supposing my observations be correct (as I hereby offer to demonstrate they are, to any one of you, on a suitable occasion), I show first by my own experiments that white blood-corpuscles as drawn from the vessels, if submitted to the action of diluted serum, assume the form and characters of salivary globules; second, by the aid of the investigations of Cohnheim and others, I point out an obvious way by which these same white blood-corpuscles constantly escape from the blood-vessels, and make their way into the salivary fluid; and lastly, prove by direct experiment the converse of my first proposition, namely, that salivary globules, when exposed to the influence of a stronger salt solution having the exosmotic power of the blood serum, contract to the size of white blood-corpuscles, and take on (rather let me say *resume*) their characteristic amœboid movement. I therefore conclude that my theory, first propounded in 1869, that the corpuscles of the saliva are "migrating" white blood-globules, which, "wandering out" into the oral cavity, have become distended by the endosmosis of the rarer fluid in which they float, may now be considered established upon a firm experimental basis.

Finally, let me remark that, although some persons may be inclined to query of what benefit this item of information in regard to the salivary globules will be to practitioners of dentistry and other medical men, I have no doubt that, either alone or linked with other facts, it will soon cast some light upon pathological processes in the mouth which are now more or less obscure. It is related that upon a certain occasion, some one, in the presence of the celebrated Coleridge, undervalued the importance of a new discovery, by exclaiming "What of it? it is of no use to the world," and that the poet justly rebuked this caviller, by asking him "Of what use is a new-born child?" A hundred and forty odd years ago the same question might have been put to Augustine and Mary Washington about their infant, then, as the great dramatist describes it, "mewling and puking in his nurse's arms," the new-born son of their house; and at that moment the acknowledgment must have been made that he was absolutely of no use in the world; yet if we look abroad to-day at the millions of free, happy, and industrious citizens who crowd the farms, the factories, the workshops, and the commercial marts throughout the length and breadth of our Union, the answer comes to us with trumpet tones that the man who developed from that child was, through the providence of God, in his day and generation, the most useful that the world has ever seen.

And so, gentlemen, is it with *all* the apparently useless researches of philosophers into the arcana of nature. We can never foresee what advantage a consciousness of any particular "downright fact" will be

to us in the dim and distant future; but "Knowledge is *always* power," and we may be sure that every honest and faithful observation of physical phenomena which arise from the action of those unchangeable, but infinitely various and conflicting laws that govern force and matter, will sooner or later, directly or indirectly, contribute towards extending that knowledge of man, in his countless complex relations, which constitutes the proper study of all mankind.